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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,951	10/13/2000	Jeffrey L. Cleland	GEN02-002-US	8871

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/687,951	CLELAND ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,20-23,25-31 and 33-39* is/are pending in the application.

4a) Of the above claim(s) *38* is/are withdrawn from consideration.

5)☒ Claim(s) *22* is/are allowed.

6)☒ Claim(s) *17,20,21,23,25-29,34,35 and 39* is/are rejected.

7)☒ Claim(s) *30,31,33,36 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 17, 20-23, 25-31 and 33-39 are pending.

Applicants' amendment filed on November 27, 2004 is acknowledged, and the response has been fully considered. Claims 17, 21-23, 25 and 26 have been amended, and new claims 38 and 39 have been added. Newly submitted claim 38 directed to an invention that is distinct from the invention originally claimed for the following reasons:

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 38 is withdrawn from consideration as being directed to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Thus, claims 17, 20-23, 25-31, 33-37 and 39 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 23 and 26 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendment to the claim and applicants' response at page 6 in the amendment filed November 27, 2004.

Claim Rejections - 35 USC § 102

3. The previous rejection of claims 17, 21, 25-29 and 35 under 35 U.S.C. 102(b) as being anticipated by McGinity *et al.* (US Patent 5,288,502, February 22, 1994), is withdrawn in view of applicant's amendment to the claim and applicants' response at pages 6-7 in the amendment filed November 27, 2004.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claims 17, 21, 23, 25-29, 34, 35 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Cleland *et al.* (US Patent 6,113,947, filed June 13, 1997).

Cleland *et al.* teach a nerve growth factor (NGF) microencapsulation composition having controlled release characteristics, wherein NGF is dispersed in a polymeric matrix of microspheres, microparticulates and microcapsules (column 2, lines 8-67; column 4, line 62-column 5, line 2; claims 28 and 29) and the microspheres are sieved to about 20-90 microns for injecting intramuscularly (column 19, lines 38-45; column 19, line 63-column 20, line 4; column 23, lines 53-63), and a biodegradable polymer such as a copolymer of lactic acid and glycolic acid (PLGA) is used a polymeric matrix (column 4, lines 24-32, Example 1; claims 25-27). The preferred injectable sustained-release preparation can be formulated with a viscous

physiologically acceptable solution including a dispersant such as sodium hyaluronate, a preservative, an isotonizing agent such as NaCl, and a local anesthetic to provide an aqueous suspension (column 19, lines 47-62, claims 17, 21, 23, 34, 35 and 39), where the size of microsphere (e.g., most preferably, 20-90 microns) for an injectable suspension may be selected from the range satisfying the requirement for the degree of dispersion and passage through the needle (column 19, line 63-column 20, line 4).

5. Claims 17, 21, 23, 25-28, 34 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Suzuki *et al.* (US Patent 6,197,326, filed October 14, 1998).

Suzuki *et al.* teach an intra-articular preparation for the treatment of arthropathy, which comprises microcapsules of a biocompatible, high molecular weight substance such as PLGA, homopolymer or copolymer of lactic acid, glycolic acid, caprolactone and others (column 1, lines 45-60; column 2, line 66-column 3, line 30; claims 25-27), and a drug such as steroid agents, cyclosporin (a cyclic peptide; claims 28), hyaluronic acid (column 3, lines 44-64); and the microcapsules can be administered in the form of injection by suspending it in a dispersion medium, where injection-grade water may be used as the dispersion medium, further, a buffer, an isotonicity (e.g., NaCl; claim 23), and others can be added, particularly a microcapsule-dispersing medium which contains hyaluronic acid, or chondroitin sulfate or salts thereof is particularly preferred (column 4, line 60-column 5, line 8; claims 17, 21, 34 and 39). Since the injectable intra-articular preparations are prepared by suspending microcapsules in a dispersion medium containing hyaluronic acid for injection, it would be expected that an aggregation-reducing amount of hyaluronic acid is used to maintain the suspension for injection, which meet the criteria of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 17, 20, 21, 23, 25-29, 34, 35 and 39 are rejected under 35 U.S.C 103(a) as being unpatentable over Cleland *et al.* (US Patent 6,113,947) in view of syringe section (page T515) of Aldrich catalog (1996-1997).

Cleland *et al.* teach a nerve growth factor (NGF) microencapsulation composition having controlled release characteristics, wherein NGF is dispersed in a polymeric matrix of microspheres, microparticulates and microcapsules (column 2, lines 8-67; column 4, line 62-column 5, line 2; claims 28 and 29) and the microspheres are sieved to about 20-90 microns for injecting intramuscularly (column 19, lines 38-45; column 19, line 63-column 20, line 4; column 23, lines 53-63), a biodegradable polymer such as a copolymer of lactic acid and glycolic acid (PLGA) is used as a polymeric matrix (column 4, lines 24-32, Example 1; claims 25-27), and the

preferred injectable sustained-release preparation can be formulated with a viscous physiologically acceptable solution including a dispersant such as sodium hyaluronate to provide an even suspension of the particles to avoid settling during mixing and injection (column 19, lines 47-62; column 23, lines 53-60; claims 17, 21, 23, 34, 35 and 39), where the size of microsphere (e.g., most preferably, 20-90 microns) for an injectable suspension may be selected from the range satisfying the requirement for the degree of dispersion and passage through the needle (column 19, line 63-column 20, line 4). However, Cleland *et al.* does not disclose the type of syringe needle used for injection. The Aldrich catalog shows a 23-gauge syringe needle has an inside diameter of 0.318 mm (318 microns), which is suitable for injection of the particulate preparation with particle size of 5-200 microns (claim 20). At the time of invention was made, it would have been obvious to one of ordinary skill in the art to prepare an injectable microsphere formulation as taught by Cleland *et al.* using a syringe of 23-gauge needle as indicated in the Aldrich catalog because one of ordinary skill in the art would have been motivated to deliver the formulation having even suspension of particles to a patient with the needles having the right gauge, e.g., 23-gauge or smaller. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

In response, applicants indicate Cleland *et al.* neither teaches nor suggests an injectable formulation as claimed, wherein the formulation comprises an aggregation-reducing amount of hyaluronic acid, and page T515 of the Aldrich catalog simply discloses various gauge needles and does not remedy the deficiency of Cleland, thus neither Cleland *et al.* nor the Aldrich

catalog, alone or in combination, teach or suggest an injectable formulation as claimed; Applicants have discovered that the use of hyaluronic acid in polymer-based formulations can allow the use of 23 gauge or smaller needles, and Applicants have provided working examples demonstrating that the claimed formulations can be administered in small needles (Examples 3, 4, 5, and 7); In view of the known problems with the use of smaller needles to inject polymer-based drug formulations, one of skill in the art would not have been motivated to inject the formulation through a 23 gauge or smaller needle (pages 8-9 of the response).

The response has been fully considered, however, the argument is not found persuasive because Cleland *et al.* indicate to prepare an injection formulation containing the microsphere, a viscous physiologically acceptable solution of a dispersant (i.e., hyaluronic acid) can be included in the formulation to provide an even suspension of the particles to avoid settling during mixing and injection (column 19, lines 47-62; column 23, lines 53-60), where the size of microsphere (e.g., most preferably, 20-90 microns) for an injectable suspension may be selected from the range satisfying the requirement for the degree of dispersion and passage through the needle (column 19, line 63-column 20, line 4). Thus, it would have been obvious to one of ordinary skill in the art to use an aggregation-reducing amount of hyaluronic acid in buffer to prepare the injectable microsphere formulation having even suspension and to administer the preparation using the syringe with right gauge (e.g., 23-gauge or smaller). Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Claim Objections

7. Claims 30, 31, 33, 36 and 37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

8. Claims 17, 20, 21, 23, 25-29, 34, 35 and 39 are rejected, and claims 30, 31, 33, 36 and 37 are objected to. It appears claims 22 is free of art and are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. CMK
Patent Examiner

CMK
February 10, 2005

JON WEBER
SUPERVISORY PATENT EXAMINER